REMARKS/ARGUMENTS

Claim Status/Support For Claim Amendments

In response to the Office Action of May 7, 2003, Applicants request re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

No new matter has been added by the amendments to the specification.

A substitute Sequence Listing was provided in order to add predicted amino acid residues disclosed in the figures.

The Brief Description of the Figures was amended to add sequence identifiers for the sequences disclosed in the figures.

A protocol in the experimental section of the detailed description has been amended to properly identify the trademark SEPHAROSE using capitalization.

The abstract has been amended to remove the legal phraseology ("said").

Claim 1 has been amended. Claims 2-35 have been canceled. Claims 36-43 have been added. Claims 1 and 36-43 are pending in the instant application. As stated herein under the heading **Restriction/Election** (se p.10), the election of the Group I invention is affirmed, claim 1 now constituting said Group I invention. As later explained, if this claim is deemed to be allowable, rejoinder of the remaining claims in accordance with *Ochiai* is respectfully requested.

No new matter has been added by the addition of new claims 36-43. The subject matter of new claims 36-43 corresponds to the subject matter of canceled claims 3-28. The above additions to the claims also find basis in the original disclosure at page 12, lines 2-12; page 17, lines 7-14; page 18, lines 5-7 and page 27, lines 17-23. The method of claims 36-40 is described in detail at pages 20-27. Page 28,line 9 to page 29,line 5 refers to the use of various types of samples and their measurement. Figure 1 shows data derived when using the claimed method on samples obtained from a human patient. Page 28, line 1 to page 33, line 2 describes kits and their contents contemplated for use with the claimed methods. It is clear from these specific recitations and from the description of methods utilized that the methods and types of kits were fully contemplated by the inventors at the time of filing and were enabled by virtue of the disclosure as originally filed.

Sequence Compliance

Applicants have reviewed the entire specification including the figures and the claims for sequence disclosures. The only sequence found to be disclosed is the amino acid sequence identified as SEQ ID NO:1. Applicants provided a Sequence Listing (in both paper and computer readable form) disclosing SEQ ID NO:1 on April 19, 2002. However, Applicants noted that the first and last amino acid residues of SEQ ID NO:1 (as disclosed by the

sequence shown in the figures) were not included in the originally filed Sequence Listing. Applicants herein provide a diskette containing a substitute Sequence Listing in electronic computer readable form to replace the previously submitted copy (filed on April 19, 2002). The diskette submitted herewith contains a Sequence Listing which adds the first and last amino acid residues (shown in the figures) to SEQ ID NO:1. As shown in Figure 1, the marker identified in patient sera consists of amino acid residues 2-13 of SEQ ID NO:1. When carrying out mass spectrometric procedures, it is possible to fragment a whole molecule, depending upon the enzyme used for digestion. A sequence is often predicted from these fragments but often the sequence is not identified completely. It is conventional in the art to show the missing portions of the predicted sequence in parentheses. The first (R) and last (D) amino acid residues of SEQ ID NO:1 are predicted residues as indicated by the parentheses in Figure 1. The peptide sequence without the predicted first and last amino acid residues was shown in the original specification at page 27, line 18 and is shown in the figures with the first and last predicted amino acid residues. Thus, no new matter is added, the substitute Sequence Listing is for the purpose of clarifying the use of parentheses only. Applicants also herein provide a substitute paper copy of the Sequence Listing as contained on the diskette filed herewith. The computer readable form of the substitute Sequence Listing is

identical to the paper copy of the substitute Sequence Listing. The amendments to the claims and specification limiting the marker sequences to specific amino acid residues are also made for the purpose of clarification only. The claims as herein amended limit the marker sequence to amino acid residues 2-13 of SEQ ID NO:1.

Restriction/Election

Applicants herein affirm the election of Group I (claims 1, 2 and 10-28) without traverse for prosecution on the merits. The election was made during a telephone conference with the Examiner on April 14, 2003.

The instant application is related in claim format to several pending applications of which serial number 09/846,352 is exemplary. The biopolymer marker of serial number 09/846,352 was found to be novel and subsequently claims reading on methods and kits limited to its use were rejoined with the claims reading on the biopolymer marker under *Ochiai*. In an effort to maintain equivalent scope in all of these applications, Applicants respectfully request that the Examiner enter new claims 36-43 in the instant application and consider joining them (new claims 36-43) with the claims of the elected invention (Group 1) *upon the Examiner's determination that* the claims of the elected invention are allowable, since if the peptide consisting of amino acid residues 2-13 of SEQ ID NO:1 is found to be novel, methods and kits limited to its use should also be found novel.

Rejections under 35 USC 112 (second paragraph)

Claims 1, 2 and 10-28, as originally presented, stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner alleges that claims 1 and 18 are vague and indefinite with respect to the recitation of the phrase "indicating at least one particular disease". The Examiner alleges that it is unclear what particular disease applicant refers to.

Claim 18 has been canceled and claim 1 has been amended to clearly indicate that congestive heart failure is the disease state referred to. Additionally, the phrase "indicating at least one particular disease" is not recited in any of the remaining pending claims.

The Examiner alleges that claims 10, 18 and 25 are vague and confusing with respect to the recitation of the phrase "analyte thereof". The Examiner alleges that it is unclear what analyte applicants are referring to, i.e. what type of analyte for a specified amino acid.

Claims 10, 18 and 25 have been canceled and the phrase "analyte thereof" is not recited in any of the remaining pending claims.

The Examiner alleges that the phrase "wherein the sample"

lacks antecedent basis in claims 15 and 16.

Claims 15 and 16 have been canceled, thus rendering this rejection moot.

The Examiner alleges that claims 17 and 18 are vague and indefinite with respect to the recitation of the phrase "wherein said marker".

Claims 17 and 18 have been canceled and the phrase "wherein said marker" is not recited in any of the remaining pending claims.

The Examiner alleges that claims 17 and 25 are vague and confusing with respect to the recitation of the phrase "specific therefor".

Claims 17 and 25 have been canceled and the phrase "specific therefor" is not recited in any of the remaining pending claims.

The Examiner alleges that claims 18, 26 and 27 are vague and indefinite with respect to the recitation of the phrase "therapeutic avenues related to a disease state". The Examiner alleges that it is unclear what disease applicant refers to and it is further unclear what "therapeutic avenues" refers to.

Claims 18, 26 and 27 have been canceled and the phrase "therapeutic avenues related to a disease state" is not recited in any of the remaining pending claims.

Accordingly, applicants have now clarified the metes and bounds of the claims and respectfully request that the above-discussed rejections under 35 U.S.C. 112 (second paragraph) be

withdrawn.

Rejections under 35 USC 102(a) and (b)

Claims 1 and 2, as originally presented, stand rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Bar-Or *et al.* (WO 01/25265 A1).

The Examiner alleges that the Bar-Or reference is an invention relating to metal binding peptides that prevent damage by reactive oxygen. The Examiner further alleges that Bar-Or teach a sequence of polypeptides comprising the instantly claimed SEQ ID NO:1 as a reactive species inhibitory protein (see Example 10, page 43 of Bar-Or).

Claim 2 has been canceled and claim 1 has been amended herein to recite a specific peptide (amino acid residues 2-13 of SEQ ID NO:1) with a specific function (diagnostic for congestive heart failure).

In order to anticipate a claim, the reference must teach every element of the claim (see MPEP 2131). The Bar-Or reference teaches a method for reducing the damage done by reactive oxygen species (ROS) in an animal (see Bar-Or abstract). The Bar-Or reference teaches the same peptide as the instantly claimed peptide (page 43 of Bar-Or); however Bar-Or tests the peptide for its ability to inhibit the production of reactive oxygen species. No where does the Bar-Or reference teach that the peptide or any portion thereof

can be diagnostic for congestive heart failure. The instant claim as amended herein requires that the peptide be diagnostic for congestive heart failure.

Accordingly, Applicants respectfully submit that the claim, as instantly presented, now distinguishes over the composition taught by Bar-Or *et al.* and respectfully request that this rejection be withdrawn.

Claims 1, 2, 10-14, 17-22 and 25-26, as originally presented, stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Bar-Or *et al.* (WO 00/20840).

The Examiner alleges that the Bar-Or reference teaches the following; rapid methods for the detection of ischemic states and kits for use in such methods and a sequence of polypeptides comprising the instantly claimed SEQ ID NO:1 as the measurement of an ischemic event (see example 32, page 60 of Bar-Or).

The Examiner further alleges that the Bar-Or reference teaches diagnostic assay kits comprising the instantly claimed SEQ ID NO:1 as the binding partner to detect ischemic events for clinical monitoring purposes (see Figure 3, claims 47-56, page 19, line 25-page 22, line 3 of Bar-Or *et al.*). Bar-Or *et al.* teach using a conventional ELIZA, sandwich assay and mass spectrometric analysis as the detecting means to determine the binding level from a patient's serum or plasma sample (see examples 13-17, claim 11 of

Bar-Or). Bar-Or *et al.* teach immobilized monoclonal antibodies, i.e. sequence specific for N-terminus polypeptide (as the instantly recited SEQ ID NO:1) on a solid support (see claim 56 of Bar-Or). The Examiner alleges that although Bar-Or do not specifically teach using a labeled antibody, it is an inherent contemplation ordinary in the art of immunoassay, including sandwich, ELISA or enzyme assay (see page 19, line 25-page 21, line 30 of Bar-Or).

Claims 2, 10-14, 17-22 and 25-26 have been canceled. New claims 41-43 are drawn to diagnostic kits. Claim 1 has been amended herein to recite a specific peptide (amino acid residues 2-13 of SEQ ID NO:1) with a specific function (diagnostic for congestive heart failure).

In order to anticipate a claim, the reference must teach every element of the claim (see MPEP 2131). The Bar-Or reference teaches rapid methods for the detection of ischemic states and also teaches kits for use in such methods (see abstract of Bar-Or). The Bar-Or reference teaches the same peptide as the instantly claimed peptide (page 60 of Bar-Or); however Bar-Or tests the ability of metals to bind to the peptide. No where does the Bar-Or reference teach that the peptide or any portion thereof can be diagnostic for congestive heart failure. The instant claims as amended herein require that the peptide be diagnostic for congestive heart failure. Additionally, new claims 41-43 are drawn to kits specifically for the diagnosis of congestive heart failure.

Accordingly, Applicants respectfully submit that the claims, as instantly presented, now distinguish over the compositions and kits taught by Bar-Or *et al.* and respectfully request that this rejection be withdrawn.

Rejection under 35 USC 103(a)

Claims 15, 16, 23, 24, 27 and 28, as originally presented, stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Bar-Or *et al.* (WO 00/20840) in view of Hutchens *et al.* (US 6,225,047 B1).

The Examiner alleges that the Bar-Or reference does not teach obtaining patient samples in an unfractionated body fluid, a tissue sample or nature body fluids (Bar-Or teaches fractionating samples).

The Hutchens reference is deemed to teach a method and kit for identifying biopolymer markers representative of or capable of categorizing specific disease states using SELDI-MS. Hutchens *et al.* also teach that the sample choice could be from unfractionated body fluids such as blood, urine, blood products or tissue samples. The method and kit of Hutchens *et al.* may be applied to multiple samples at different times (see column 8, lines 45-53 of Hutchens *et al.*).

The Examiner alleges that it would have obvious to one of ordinary skill in the art at the time that the instant invention

was made to make a diagnostic assay kit in combination of the teaching of Bar-Or *et al.*, i.e. SEQ ID NO:1 which comprises a biopolymer used as a diagnostic marker of a disease state (ischemic event) with the range of sample choice as taught by Hutchens *et al.* since economy of convenience is routine in clinical practice.

Claims 15, 16, 23, 24, 27 and 28 have been canceled. New claims 41-43 are drawn to kits specifically diagnostic for congestive heart failure. Even if one of ordinary skill in the art were to use an unfractionated sample (as taught by Hutchens *et al.*) in the methods and kits of Bar-Or *et al.* one would not arrive at the instant invention, since the instant invention as herein claimed is drawn to diagnostic kits specific for congestive heart failure. Neither Bar-Or *et al.* or Hutchens *et al.* teach or suggest any method, polypeptide or kit diagnostic for congestive heart failure.

It is respectfully submitted that the ordinary skilled artisan, having both references in front of him/her (Bar-Or *et al.* and Hutchens *et al.*) would not be motivated to use an unfractionated sample with a kit diagnostic for congestive heart failure.

Thus, it is respectfully submitted that the combination of Bar-Or *et al.* in view of Hutchens *et al.* fails to reasonably teach or suggest to one of ordinary skill in the art the elements of the invention as specifically set forth in the instantly amended

claims.

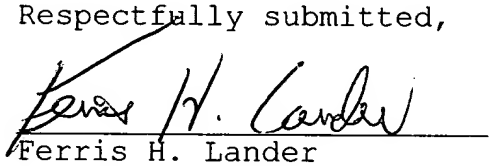
Declaration Under 37 CFR 1.132

A declaration under 37 CFR 1.132 is filed concurrently herewith in order to provide evidence of the absence of the 1406 dalton biopolymer marker(amino acid residues 2-13 of SEQ ID NO:1) in normal human sera.

CONCLUSION

In light of the foregoing remarks, amendments to the specification and amendments to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,



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